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Patient Pretreatment Evaluation and Monitoring

Policy: LTBI must be diagnosed and active TB Disease ruled out prior to initiating treatment the patient should be evaluated at least monthly during treatment.

Purpose: To ensure safe and appropriate treatment for LTBI.

Procedure:

1. **Rule out active TB Disease:** TB Disease must be ruled out before treatment for LTBI is started. Ensure that the patient has received a medical evaluation and CXR to rule out active TB Disease. The TB signs and symptoms checklist should be completed initially on each individual with a positive TST or IGRA. If patient is symptomatic, collect three sputums and submit to the State Public Health Lab for evaluation. Collect three sputums; one early morning and all three must be eight hours apart. If cultures are pending, wait for results even if sputum results are smear negative. Submit sputums to State Public Health Lab (See Chapter 3).

2. **Clinical Monitoring:** Schedule a visit with the patient (home or clinic) at least monthly to include:
   - Brief physical assessment for signs of hepatitis (see Appendix 8: Urine Chart/Patient Information Card)
   - Assessment of adherence to treatment
   - Review of symptoms for possible adverse medication reactions or interactions
   - Review of signs and symptoms of TB Disease.

3. **Patients should be instructed initially and at each monthly visit to stop taking TB medications and to seek medical attention immediately if symptoms of hepatitis develop and not to wait until a clinic visit to stop medications.**

4. **Liver Function (LFT) Testing:**
   a. Baseline AST/SGOT, ALT/SGPT at the start of LTBI therapy is recommended for patients with any of the following:
      - Liver disorders
      - History of liver disease (hepatitis B or C, alcoholic hepatitis or cirrhosis)
      - Regular use of alcohol
      - Risks for chronic liver disease
      - HIV infection
      - Pregnancy or the immediate postpartum period (within 3 months of delivery)

b. Baseline testing can be considered on an individual basis, especially for patients taking other medications for chronic medical conditions. LFT's will only be covered by the Diagnostic Services Program (DSP) on a case by case basis, with prior approval by the DHSS TB Control Program. (See TB Manual- DSP Program)

c. Routine periodic retesting is recommended for individuals with abnormal initial results and other persons at risk for hepatic disease.

d. Laboratory testing is recommended for any patient who has symptoms suggestive of hepatitis such as:

Fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, dark urine, chills, or signs of jaundice

e. AST level 3 or more times the upper limit of normal can be accepted if the patient is free of hepatitis symptoms, and up to 3 times the upper limit of normal if there are signs and symptoms of liver toxicity

***Also see *MMWR Treatment of Tuberculosis* at:**
http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf Page 43- Section 6.3.4 Hepatitis

5. Patient Education:

a. Explain the disease process and rationale for medication in the absence of symptoms or CXR abnormalities.

b. Provide patient education, written and verbal instructions, in patient's primary language, if available.

c. Advise the patient to abstain from the consumption of alcohol, to include beer and wine. The combination of alcohol and TB medications together can cause life threatening liver conditions.

d. Reinforce patient education at each visit.

e. Ensure confidentiality.

f. Review the importance of completing treatment for LTBI.

6. **Discuss Management of Common Side Effects Assessing Adherence:**
    a. Many variables affect a patient's adherence to the medication regimen for treatment of LTBI. Episodes of non-adherence should be addressed as soon as possible.

    b. Adherence Questionnaire:
        - When do you take your medicines?
        - How do you remember to take your medicines?
        - How many pills did you miss?
        - How many pills do you have left in your medication bottle?
        - When was the last time you missed any of your LTBI medications?

    c. Request patient to bring medication bottles with them to each clinic visit. Count remaining pills in each bottle.

    d. Discuss patient reminders such as pill boxes or calendars to increase adherence to medication regimen.

7. **Directly Observed Therapy (DOT)** should be considered under the following circumstances:
    a. Medication is prescribed intermittently. There are several treatment regimens available for the treatment of LTBI. Providers should choose the appropriate regimen based on:
        - Drug-susceptibility results of the presumed source case (if known);
        - Coexisting medical illnesses; and
        - Potential for drug-drug interactions.

    b. For persons who are at especially high risk for TB disease and are either suspected of non-adherence or are given an intermittent dosing regimen, directly observed therapy (DOT) for LTBI should be considered (**for more information on DOT, see the *TB Manual*; *Case Management: Disease* located at:** http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Chap4.pdf). This method of treatment is especially appropriate if the person in need of LTBI treatment lives with a household member who is on DOT for TB disease, or lives in an institution or facility where treatment for LTBI can be observed by a staff member. It is necessary to exclude TB disease before starting LTBI treatment.

    c. The patient is high risk (HIV positive, TB contact or child < 5 years of age.)

8. **Dispensing TB Medications:**
   a. Ensure the five rights of medication administration are followed: Right patient, right medication, right time, right dose and right route.

   b. Check patient allergies.

   c. Do not issue more than a 30- day supply of medication at each monthly clinic visit.

   d. Medication may be transferred to another agency that will be providing DOT for the patient i.e. long-term care facility, detention center, school or university. Notation of the transfer of medication should be documented in the patient record and DHSS's TB Control Program shall be notified. LPHA staff are responsible for monthly follow up of all patients receiving LTBI treatment.

9. **Documentation of Clinic Visit:**
   a. If it is not documented, it did not happen.

   b. Signs/symptoms of adverse reactions must be documented with actions taken in the patient record.

   c. Information can be entered into the encounter page of the WebSurv program.

   d. Information is to be documented on page 2 (backside) of the TBC-4.

   e. Send a copy of the completed TBC-4 to the DHSS's TB Program if not entered in WebSurv.

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LTBI Treatment Regimens

Policy: All individuals taking treatment for LTBI should be on a standard treatment regimen as indicated by the CDC/ATS recommendations.

Purpose: To ensure safe and appropriate treatment for LTBI.

Reference: Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection (MMWR 200: 49 (No. RR-6)): http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm
http://www.cdc.gov/tb/publications/reportsarticles/mmwr/mmwr_updates.htm

Treatment Regimens

Drug/Dose	Frequency/Duration
Isoniazid Adult: 5 mg/kg Children: 10-15 mg/kg Maximum dose 300 mg	Daily x 9 months (CDC preferred regimen)
Isoniazid Adult: 15 mg/kg Children: 20-30 mg/kg Maximum dose 900 mg	Twice weekly x 9 months by DOT
Isoniazid Adults: 5 mg/kg Maximum dose 300 mg	Daily x 6 months
Isoniazid Adults: 15 mg/kg Maximum dose 900 mg	Twice weekly x 6 months by DOT Once weekly x 12 weeks by DOT in combination with Rifapentine
Rifampin Adults: 10 mg/kg Children: 10-20 mg/kg Maximum dose 600 mg	Daily x 4 months
Rifapentine Adults: 10-50 mg/kg Children: 10-50 mg/kg (≥12 yrs old) Maximum dose 900 mg	Once Weekly x 12 weeks by DOT in combination With Isoniazid

Peripheral Neuropathy

- Uncommon at doses of 5 mg/kg
- Those at risk may also be given pyridoxine (vitamin B6)
  - Persons at high risk for neuropathy (e.g., diabetes, uremia, alcoholism, malnutrition, HIV infection)
  - Pregnant women » Persons with a seizure disorder
  - Patients who develop signs and symptoms of peripheral neuropathy

Medication Fact Sheets: (**see the *TB Manual*; *Appendices/Educational Materials* located at**: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

Checklist for Latent TB Infection - (**see the *TB Manual*; *Appendices/Other Resources* located at**: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

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LTBI Medications – Adverse Effects

Policy: To educate the patient concerning the adverse effects of medications used for the treatment of LTBI.

Purpose: To ensure the patient has education concerning the adverse effects of TB medications and what action to take.

NOTE: Patients should be instructed initially and at each monthly visit to stop taking TB medications and to seek medical attention immediately if symptoms of hepatitis (liver toxicity) develop and not to wait until a clinic visit to stop medications.

Possible adverse effects of INH:

- Asymptomatic elevation of liver enzyme concentrations (LFT's) occur in 10 – 20% of people taking INH. Increased enzyme concentrations can be accepted up to 5 times the upper limit of normal for patients who are free of hepatitis symptoms. Liver enzyme concentrations usually return to normal even when treatment is continued.

- Risks of fulminant INH-related hepatitis appears to be greatest if INH is continued after onset of symptons of hepatotoxicity. (In one study, 7 of 8 patients requiring INH related liver transplant continued taking INH for at least 10 days after onset of symptoms.

- Clinical monitoring is based on educating patients about the symptoms of hepatotoxicity and instructing them to stop treatment immediately if such symptoms occur and report to the clinician for evaluation.

- Clinical hepatitis occurs in 0.1% to 0.15% of people taking INH, and is more common when INH is combined with other agents. Factors that may increase either these rates or the severity of the hepatitis include alcohol consumption, underlying liver disease or risks for liver disease and the concurrent use of other medications which are metabolized in the liver such as Ascetomenaphin.

- Peripheral neuropathy, caused by interference with metabolism of Vitamin B6 (pyridoxine) can occur in less than 0.2% of people taking INH at regular doses (300 mg a day), and is more likely in the presence of other conditions associated with neuropathy such as diabetes, HIV, renal failure and alcoholism.

- Adverse effects of INH: Neuropathy when taking INH, 10-50 mg of Vitamin B6 (pyridoxine) supplementation is recommended for:
    a. Pregnant or breastfeeding women.
    b. Individuals with seizure disorders.
    c. Patients with conditions in which neuropathy is common (e.g. diabetes, uremia, alcoholism, malnutrition, HIV infection).

In practice, B6 is often given to all patients taking INH (typically 25-50 mg/day).

Possible adverse effects of Rifampin:

1. Hepatotoxicity, may occur in 0.6% of persons taking Rifampin. Hepatitis is more likely when combined with INH.

2. If not able to tolerate INH (elevated LFT) can often tolerate Rifampin.

3. Cutaneous reactions, such as flushing and itching with or without a rash, may occur in 6% of persons taking Rifampin. It is generally self-limiting and may not be a true hypersensitivity; continue treatment if possible.

4. Gastrointestinal symptoms such as nausea, anorexia, diarrhea and abdominal pain are rarely severe enough to discontinue treatment.

5. Reddish orange to reddish brown discoloration of body fluids (urine, stool, saliva, sputum, sweat and tears) is expected and harmless, but patients should be advised. Soft contact lenses may be permanently stained.

6. Rifampin interacts with a number of drugs, causing drug-drug interactions. It is known to reduce concentrations of oral hypoglycemic agents, methadone, warfarin, oral contraceptives and phenytoin. Women using oral or other systemic hormonal contraceptives are at greater risk of becoming pregnant during Rifampin therapy; therefore these patients should use additional forms of contraception such as condoms.

7. Thrombocytopenia (low platelets) is a possible adverse reaction to Rifampin. Complete Blood Count (CBC) and platelets at baseline may be indicated. It has occurred primarily with high dose intermittent therapy or after resumption of interrupted therapy. It rarely occurs at 10 mg/kg dose and is reversible if Rifampin is discontinued as soon as purpura (bruising) occurs.

8. Rifampin is contraindicated in HIV infected patients being treated with certain protease inhibitors (PI) or nonnucleoside reverse transcriptase inhibitors (NNRTI). In this situation, Rifabutin may be substituted.

Interruption of Therapy

Policy: To provide the client with the recommended treatment for LTBI when interruptions of therapy occur.

Purpose: To provide recommendations on how to ensure the client receives the recommended doses of medication to complete therapy.

Procedure:

1. Completion of Therapy is based on the total number of doses administered – not on duration of therapy alone.
    a. The 9 month regimen of daily INH consists of 270 doses, at minimum, administered within 12 months
    b. The 6-month regimen of INH consists of 180 doses administered within 9 months.
    c. The twice weekly INH regimen consists of:
        - At least 76 doses administered within 12 months or *
        - At least 52 doses administered within 9 months *
    d. The 12 dose weekly regimen consists of:
        - Patient must complete 11 of 12 doses to be considered complete **

2. Ideally, the patient should receive medication on a regular dosing schedule until completion of the indicated course of therapy. However, in practice some doses may be missed, requiring the course to be lengthened.

3. When restarting therapy for patients who have interrupted treatment, clinicians may need to continue the regimen originally prescribed or renew the entire regimen if interruptions were frequent enough to preclude treatment doses as recommended above.

4. If greater than a 2-month interruption of therapy occurs, a medical examination to rule out active TB disease is indicated.

***Intermittent regimen should be given utilizing DOT**.
****12 dose regimen must be given by DOT**.

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Special Considerations in Treatment of LTBI

Policy: To provide appropriate treatment for LTBI for all individuals.

Purpose: To address special conditions while treating individuals for LTBI.

Contacts to Cases:

1. Contacts are those with recent, prolonged exposure to a person with known or suspected infectious TB. They should be evaluated immediately for TB Disease and LTBI.
2. If TST or IGRA is positive, LTBI treatment guidelines should be followed, after ruling out active TB disease
3. If TST or IGRA is negative, the contact should be retested in 8 – 10 weeks.
4. Window Treatment: If a contact is a child less than 5 years of age, an HIV positive person or other immunocompromised persons of any age, treatment should be initiated immediately until the 2nd follow up TST or IGRA is done. If negative, no further treatment for LTBI is usually indicated.
5. DOT is recommended for infected contacts of active disease cases.

Re-Infection:

In general, TSTor IGRA positive contacts with a **documented** history of prior adequate treatment for LTBI do not need to be retreated. Re-treatment may be indicated for persons at high risk of becoming infected and progressing to TB Disease again such as immunocompromised persons.

HIV-Positive Individuals:

1. HIV infected individuals should be treated with a 9-month regimen of INH.
2. Rifampin is contraindicated in HIV-infected person being treated with certain combinations of antiretroviral drugs. In those cases, rifabutin may be substituted for Rifampin. See CDC website: www.cdc.gov/tb
3. If TST or IGRA is negative, treat if person has recent, prolonged exposure to infectious TB or if there is ongoing risk for exposure.

Pregnancy:

1. Consider immediate treatment for LTBI if the woman is HIV-infected or recent contact to infectious case.
2. In the absence of risk factors for active TB, wait until three months post partum to avoid administering unnecessary medication during pregnancy.
3. INH daily or twice weekly by DOT is the preferred regimen.
4. Supplementation with 50 mg of vitamin B6 is recommended.

Breastfeeding:

1. Breastfeeding is **NOT** contraindicated in women taking INH.
2. Supplementation with 50 mg of vitamin B6 is recommended for nursing women and breastfed infants.
3. Amount of INH in breast milk is inadequate for treatment of infants exposed to TB.

Infants and Children:

1. Infants and children under 5 years of age with LTBI have been recently infected and, therefore, are at high risk for progression to disease.
2. Risk of INH-related hepatitis in infants, children and adolescents is minimal.
3. Routine monitoring of serum liver enzymes is not necessary.
4. DOT is the standard of care.

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Post-Treatment Follow-Up

Policy: All individuals completing a course of treatment for LTBI will be provided documentation of that treatment.

Purpose: To ensure that the patient has a record of LTBI treatment.

Procedure:

1. Patient should receive documentation of TST/IGRA results and treatment completion that includes: names and doses of medications, date of test, administered and read, date of CXR and date started treatment and completed. A copy of the TBC-18A may be given to the patient in addition to the TBC-18 skin testing record. **(see the *TB Manual*; *Appendices/Sample Forms* located at**: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

2. The patient should be instructed to present this documentation that they should not receive another skin test any time future testing is required. See annual statement for tuberculin reactors.*

3. Patients should be re-educated about the signs and symptoms of TB disease and told to contact his/her medical provider or local health department should any of these symptoms develop.

4. **Routine CXRs are NOT needed, regardless of whether the patient completes treatment for LTBI. A CXR is indicated if the patient develops signs or symptoms of TB Disease.**

***Annual Statement for Tuberculin Reactors Form**: **- (see the *TB Manual*; *Appendices/Sample Forms* located at**: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

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Declining Treatment for LTBI

Policy: Treatment for LTBI is recommended to every person who is diagnosed with latent TB infection.

Purpose: To ensure that each person has the opportunity to receive education to make an informed decision about receiving treatment for LTBI.

Procedure:

1. Ensure the patient has received a medical evaluation and CXR to rule out active TB Disease.

2. Educate the patient concerning the risks and benefits of receiving treatment for LTBI.

3. Provide written TB educational materials for the patient, in their primary language, if available.

4. Allow the patient an opportunity to ask questions.

5. Have the patient sign the document: "Declining Treatment for LTBI", and place this document in the patient's record. If the patient agrees to take the treatment, have them sign the INH Medication Fact Sheet and keep in the patient's record also give the patient a copy to take with them (see the ***TB Manual*; *Appendices/Sample Forms* located at**: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

If after starting treatment the patient decides they no longer wish to take the medication, have them sign the Declining Treatment for LTBI and attach to the signed Fact Sheet and keepdeclines after starting treatment have them

6. Explain to the patient that if they change their mind concerning taking treatment for LTBI, they should contact their local health department.

Refusal of LTBI Treatment Form (TBC-2): (see the *TB Manual*; *Appendices/Sample Forms* located at: http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

Tuberculois TB Testing Record Form (TBC- 4): (see the *TB Manual*; *Appendices/Sample Forms* located at:
http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

INH/Rifapentine 12-Dose Medication Authorization Form (see the *TB Manual*; *Appendices/Sample Forms* located at:
http://health.mo.gov/living/healthcondiseases/communicable/tuberculosis/tbmanual/pdf/Appendices.pdf)

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